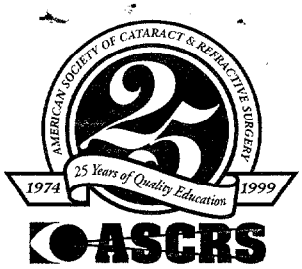

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January 12, 2000

Dockets Management Branch
Division of Management Systems and Policy
Office of Human Resources and Management Services
Food and Drug Administration
5630 Fishers Lane
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Rockville, MD 20852

RE: Docket Number 99D-4054

The American Society of Cataract and Refractive Surgery (ASCRS) appreciates the opportunity to submit comments on the agency's draft Intraocular Lens Guidance Document released for comment on October 14, 1999.

ASCRS represents nearly 8,000 ophthalmologists in the United States and abroad who share a particular interest in cataract and refractive surgical care. ASCRS members perform the vast majority of the cataract procedures done annually in the United States.

This document was reviewed by members of the society's Cataract Special Interest Group, as well as other members with extensive knowledge regarding intraocular lenses (IOLs). Following are several areas of concern identified during this review.

Our first area of concern pertains to section VII-C, subsection 2 - Data analysis tables (page 25). Under the list of clinical bullet points associated with potential implant-related problems, there should be included a category for unwanted optical images, such as glare, halos, etc. This has become an increasingly important visual characteristic associated with the performance of an IOL, and it should be recorded in the data analysis tables. This same concern can also be found in ANNEX C – Sample Package Insert, Clinical Trial (page 56). We believe that in addition to visual acuity, a statement should be made with regard to the overall optical performance of the

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implant. In particular, the occurrence of unwanted optical images such as glare and halos should be included.

ASCRS is pleased to see the discussion of lens power constants included in section VIII – Labeling (page 31). We congratulate the FDA on the emphasis included in this draft document toward establishing a clinically proven power constant prior to disseminating a new implant. The term "constant," however, is a bit of a misnomer since this factor is actually inconstant. For example, on page 32, paragraph 4, the draft guideline states "If a sponsor chooses to place their lens power constant in their labeling ..." This implies that the labeling of a specific lens power constant may not be required of all implants and manufacturers. We believe that this should be required of all new IOLs. The way in which the draft guidance document describes the protocol to derive this "constant" is quite reasonable.

In addition, we would like to recommend the following changes to section VIII. Specifically, we would suggest that the third paragraph of page 31 be reworded, with additions to the guidance document noted in italics as follows:

> For a variety of reasons, currently available *sponsors' applied* lens power constants lack sufficient consistency *so* that the above description of equivalence *may not be* assured. With a given surgical procedure, differences in measuring technique and equipment *for the preoperative eye can* create large systematic discrepancies between sites. These systematic differences *may* affect the *accuracy of the* sponsors' supplied lens power constants. Although a sponsor can determine a mean power constant with *a degree of* statistical confidence, these systematic discrepancies *can create a variance of the lens power constants for* any particular setting or facility. Authors of the different formulas recommend "personalization" of the power constant to reduce the systematic errors. This FDA guidance is intended to minimize the variation of these biases from sponsor to sponsor, at least for new lens models. However, it does not remove the need for such personalization.

Also, on page 33, under the heading Conversion from the manufacturer's choice of lens power constant to other constants, the last sentence in the first paragraph, the words "outside to" should be "outside of."

Another point of concern included in section VIII can be found on page 34 under the section titled Warning. Specifically, the guidance document states "This lens is not intended, nor should it be used, for a clear lens exchange." This is obviously a significant statement refuting the use of an IOL in the setting of a clear lens extraction. It in essence handcuffs a surgeon from performing a clear lens extraction – an important procedure in our armamentarium of refractive operations. This statement then would create a marked

liability for those surgeons who perform clear lens exchanges and implant IOLs. Either the statement should be completely deleted, or taking it one step further, a statement could be added to recognize that an implant may be used for either a clear lens exchange or cataract removal.

The next comment we would like to make pertains to Section II – Biocompatibility Testing (page 7). Specifically, in Title C, subsection 5 – ocular implant test, there is a very short section describing that the test should be performed in order to determine the tolerance of the test material after implantation in the animal eye. The draft guidance document then refers to the fact that testing should be conducted in accordance with annex F of IOS/FDIS 11979-5. Our concern with the animal testing which is required by the ISO standards are the length of time necessary for follow up of the implanted IOLs. In laboratories of ASCRS members that serve as investigators, it has been shown that adequate biocompatibility or tolerance data regarding IOL materials can be obtained in a rabbit model in as early as eight to twelve weeks. The present testing requirements for six to twelve months of testing within a rabbit eye is much too long. Not only is this a waste of time and resources, but the longer the implant remains in the rabbit eye, the more difficult it is to actually assess biocompatibility. The rabbits have a large growth of posterior cortical material as well as posterior vitreous pressure which makes the interpretation of IOL compatibility very difficult at any time beyond approximately twelve weeks. The six and twelve month evaluations show tremendous overgrowth of cortex, which may actually hinder the analysis of the IOL material rather than provide any useful information.

In addition, ASCRS would like to raise two minor points of concern. Specifically, section III – Optic Testing Subsection C, Dioptric Power (page 8). Under this section, it is interesting to note the allowed tolerance in dioptric power. As noted in the draft guidance document, almost a half a diopter range is permitted for the most commonly used implant powers. This seems a bit surprising, and it would seem that the industry would be trying to produce lenses with a much closer tolerance. Under note 2 of this section, the draft guidance document states that it is expected that manufacturers should set their tolerances to a tighter level, but perhaps this should be required.

The next minor issue is located in Section IV – Mechanical Testing and Dimensional Tolerances, subsection C, number 5, Folding/Injection testing (page 13). In the second sentence the draft guidance document states that "there should be no change in the optical and physical properties of the IOL as a result of the folding delivery." We suggest that the word "permanent" should be inserted prior to the work "change." Oftentimes, there are some temporary changes apparent in the lens optic and even haptics during folding and insertion. These changes, however, frequently dissipate rapidly, and again by inserting the work "permanent" that point could be clarified.

Lastly, ASCRS would like to provide updated information regarding references listed in section VIII – Labeling. We recommend that the 1999 and 2000 references be added on page 33 under the section Conversion from the manufacturer's choice of lens power constant to other constants as follows:

c) Holladay JT. International intraocular lens registry. J Cataract Refract Surg. 1999; 25:128-136.

d) Holladay JT. International intraocular lens registry. J Cataract Refract Surg. 2000; 26:118-134.

Again, thank you for the opportunity to comment on this draft guidance document. Should you have any questions regarding these comments, please contact Pam Johnson, ASCRS Manager of Regulatory Affairs, at (703) 591-2220 or by e-mail at pjohnson@ascrs.org.

Sincerely,

R M Sinskey

Robert M. Sinskey, MD
President